

[CASE REPORT]

Aortogenic Embolic Stroke Diagnosed by a Pathological Examination of Endovascularly Removed Thrombus: An Autopsy Report

Genki Usui¹, Hirotsugu Hashimoto¹, Yoshiya Sugiura^{1,2}, Yuji Nishi³, Masashi Kusakabe⁴, Hajime Horiuchi¹, Seiji Okubo³ and Teppei Morikawa¹

Abstract:

Complex aortic atheroma is a high-risk factor for recurrent embolic stroke. An accurate identification of stroke etiology is clinically important; however, it can be challenging. A 91-year-old man with atrial fibrillation was diagnosed with cardioembolic stroke and treated with mechanical thrombectomy. The removed thrombus microscopically contained foamy cells, suggesting an atheroembolism. An autopsy revealed an atherosclerotic lesion with ulceration, located in the aortic arch. At the lesion, the plaque had microscopically ruptured into the lumen. We therefore concluded that the aortic atherosclerotic lesion was the embolic source. Removed thrombi should be pathologically examined even if a cardioembolic stroke is clinically suspected.

Key words: aortogenic embolic stroke, complex aortic atheroma, embolism, cerebral infarction, atherosclerosis, pathology

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Introduction

Aortic atherosclerotic plaques are one of the important causes of embolic stroke (1). Complex aortic atheromas (CAAs), which are defined as plaques with a thickness >4 mm or containing mobile components or ulceration (2), are associated with a high risk of recurrent embolic stroke (3). The detection of CAAs using transesophageal echocardiography (TEE) helps to diagnose aortogenic embolic stroke (2, 4), yet accurate diagnosis is sometimes challenging, especially in patients with atrial fibrillation (AF). Recent studies have reported that histopathological findings from removed thrombi differ according to stroke etiology (5-7), yet it remains unclear whether pathological examination of a thrombus is useful for the accurate diagnosis of aortogenic embolic stroke. Here, we present a case of aortogenic embolic stroke diagnosed by the pathological examination of endovascularly removed thrombus. Pathological

examination of the removed thrombus helped to identify the stroke etiology.

Case Report

A 91-year-old man was referred to our hospital with left hemiparesis and consciousness disturbance. He had hypertension and chronic kidney disease and was taking antihypertensive drugs. He had never smoked.

At admission, he had consciousness disturbance [Glasgow Coma Scale: 10 points (E4V2M4)], conjugate eye deviation to the right, left hemiplegia, and mixed aphasia. Blood tests showed that his brain natriuretic peptide level was 283.7 pg/mL (normal: <18.4 pg/mL) and his D-dimer level was 1.4 µg/mL (normal: <1.0 µg/mL). Electrocardiography (ECG) demonstrated AF. Magnetic resonance imaging (MRI) displayed areas of high signal intensity in the right frontoparietal lobes with diffusion-weighted imaging (Fig. 1A). MRI also demonstrated an intra-arterial signal in

¹Department of Diagnostic Pathology, NTT Medical Center Tokyo, Japan, ²Division of Pathology, The Cancer Institute, Japanese Foundation for Cancer Research, Japan, ³Department of Cerebrovascular Medicine, NTT Medical Center Tokyo, Japan and ⁴Department of Radiology, NTT Medical Center Tokyo, Japan

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Correspondence to Dr. Genki Usui, gusui-ky@umin.ac.jp

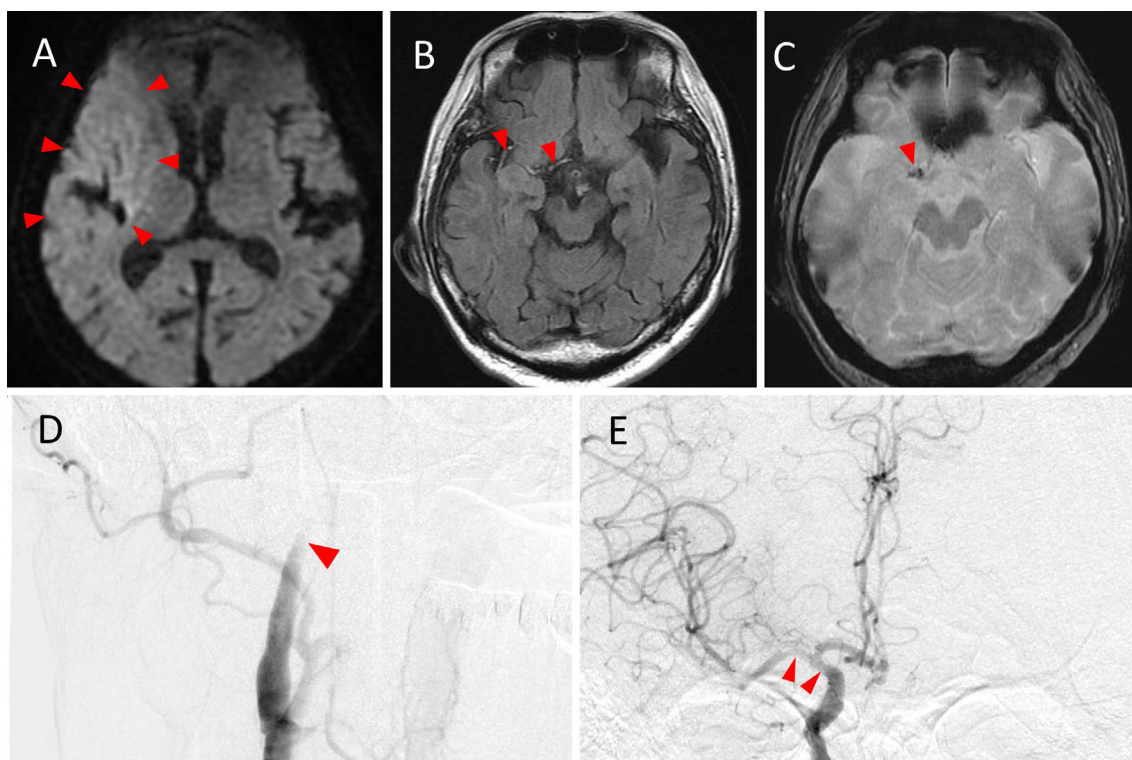


Figure 1. Magnetic resonance imaging (MRI) and cerebral angiography. **A:** MRI displays high-signal-intensity areas in the right frontotemporoparietal lobes on diffusion-weighted imaging (arrowheads). **B:** MRI demonstrates an intra-arterial signal in the right middle cerebral artery on fluid-attenuated inversion recovery (arrowheads). **C:** MRI displays a susceptibility vessel sign from the right distal internal carotid artery on T2*-weighted imaging (arrowhead). **D:** Cerebral angiography displays a filling defect at the right internal carotid artery (arrowhead) and slow flow of the distal arteries. **E:** Cerebral angiography displays the completely recanalized right distal internal carotid artery and middle cerebral artery after thrombectomy (arrowheads) (thrombolysis on the cerebral infarction scale, 3).

the right middle cerebral artery (MCA) on fluid-attenuated inversion recovery (Fig. 1B), and a susceptibility vessel sign was noted between the right distal internal carotid artery (ICA) and proximal M1 segment on T2*-weighted imaging (Fig. 1C). Magnetic resonance angiography poorly displayed the right MCA. The patient was diagnosed with acute embolic stroke. Cerebral angiography displayed a filling defect at the right ICA and slow flow in the distal arteries (Fig. 1D).

Thrombectomy was performed six hours after the “time last known well” without neurological symptoms. A thrombus was endovascularly removed, and the ICA and MCA were completely recanalized (thrombolysis on the cerebral infarction scale, 3) (8) (Fig. 1E). Plain chest computed tomography detected aortic calcification, yet carotid ultrasonography detected no embolic sources and ECG demonstrated AF. Therefore, the patient was initially diagnosed with cardioembolic stroke.

The endovascularly removed thrombus was histopathologically examined. The thrombus microscopically consisted of red blood cells and platelets within fibrin networks. Foamy cells, which are macrophages that have phagocytosed a large amount of lipids, were detected in part of the re-

moved thrombus (Fig. 2A). This finding suggested that the thrombus had been formed not in the left atrial appendage via AF but from a ruptured atheroma. Because carotid ultrasonography had not detected a thrombus in the right carotid artery, the existence of a ruptured atheroma in the more proximal carotid artery or aortic arch was suspected. The patient was treated with apixaban (10 mg/day), and stroke did not reoccur, but aspiration pneumonia developed, and he died of acute circulatory and respiratory failure 4 weeks after the thrombectomy.

An autopsy revealed necrosis of the descending colon with perforation, while no thrombus in the mesenteric artery was detected. This intestinal necrosis (non-occlusive mesenteric ischemia) was suspected to be the major cause of circulatory failure, leading to his death.

Blue toe syndrome, suggesting a cholesterol embolism, was not found. The right frontotemporoparietal lobes of the cerebrum were edematous and extensively necrosed. Embolic sources were examined, and no thrombi were found in the atrial appendage or veins of lower extremities. Nonbacterial thrombotic endocarditis was not detected. An atherosclerotic lesion with ulceration was located in the aortic arch at the orifice of the right brachiocephalic artery; no embolic

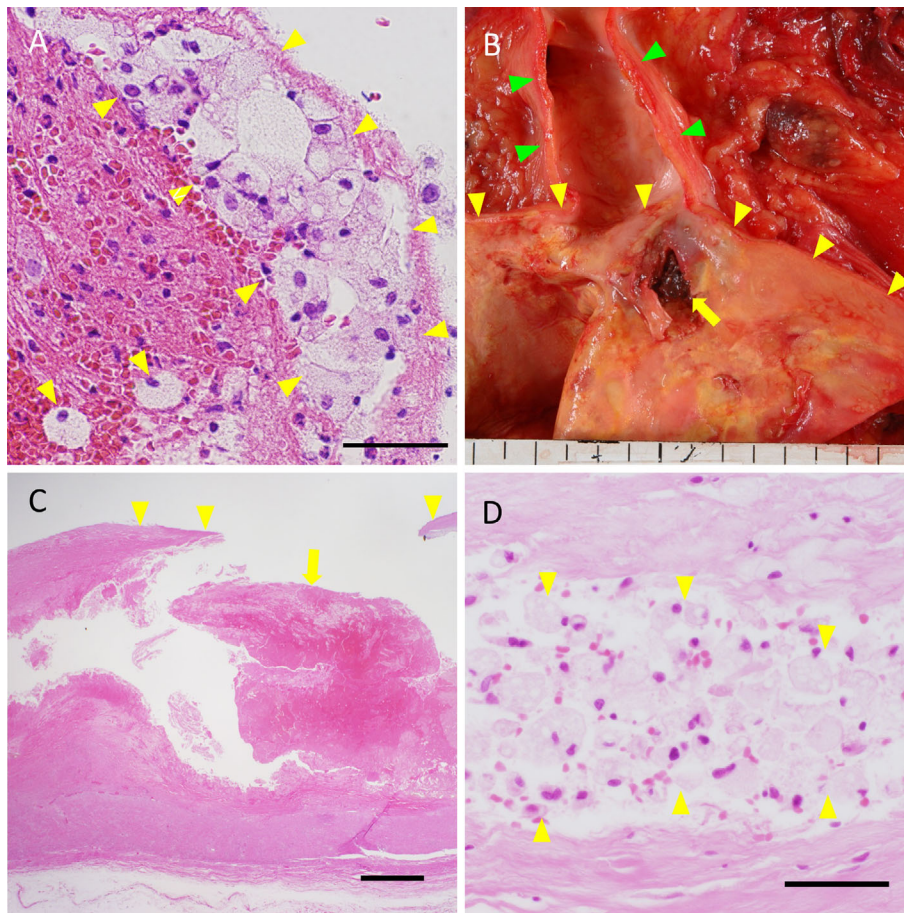


Figure 2. Thrombus and atherosclerotic lesion. **A:** The endovascularly removed thrombus microscopically contains foamy cells (arrowheads) (scale bar: 50 μ m). **B:** Atherosclerotic lesion with ulceration located in the aortic arch at the orifice of the right brachiocephalic artery (arrow). Arrowheads indicate the aortic arch (yellow) and the right brachiocephalic artery (green). **C:** Histopathology of the atherosclerotic lesion shows a thin fibrous cap is microscopically broken (arrowheads), and the plaque has ruptured into the lumen. A lipid-rich necrotic core is exposed into the lumen (arrow) (scale bar: 1 mm). **D:** The atheroma contains foamy cells (arrowheads) (scale bar: 50 μ m).

sources were found in the right carotid artery (Fig. 2B). Microscopically, the vascular media of the aortic arch were thickened. A thin fibrous cap was broken, and plaques had ruptured into the lumen. A lipid-rich necrotic core was exposed to the lumen (Fig. 2C) and the atheroma contained cholesterol clefts and foamy cells (Fig. 2D).

We therefore concluded that the atherosclerotic lesion with ulceration, located in the aortic arch, was the embolic source of cerebral embolism.

Discussion

This patient was initially diagnosed with cardioembolic stroke, but the endovascularly removed thrombus histologically contained foamy cells, suggesting atheroembolism. An autopsy revealed an atherosclerotic lesion with ulceration, located in the aortic arch at the orifice of the right brachiocephalic artery, and the patient was ultimately diagnosed with aortogenic embolic stroke. The pathological examination of a removed thrombus may help identify the stroke eti-

ology.

It is challenging to accurately diagnose an aortogenic embolic stroke in patients with AF. Although TEE or computed tomographic angiography is useful for detecting CAAs (2, 4), these are not performed in all embolic stroke patients with AF because they are invasive. A previous study showed that carotid atherosclerosis is associated with CAAs, and carotid ultrasonography, which is less invasive, is useful in screening for CAAs (9). However, in our case, carotid atherosclerosis was very mild despite the patient having CAAs, making it difficult to predict aortogenic embolic stroke from carotid ultrasonography. Even if CAAs are detected in patients with AF, identifying the true embolic source is challenging. An earlier study using TEE showed that 35% of patients with AF have CAAs (2). In cases with both AF and CAAs, it is difficult to distinguish whether a thrombus formed at the left atrial appendage or aortic arch atheroma. In our case, the endovascularly removed thrombus microscopically contained foamy cells, and an autopsy revealed an atherosclerotic lesion with ulceration located in

the aortic arch at the orifice of the right brachiocephalic artery. Therefore, we concluded that this was a case of aortogenic embolic stroke.

Although the pathological examination of endovascularly removed thrombi may help identify the stroke subtype, useful criteria have not been established. Previous studies have reported that histopathological findings from removed thrombi differ according to the stroke etiology (5-7). These studies reported that cardioembolic thrombi contain more fibrin/platelets and leukocytes and fewer erythrocytes than noncardioembolic thrombi (5-7). Conversely, other studies have reported that cardioembolic thrombi contain more erythrocytes than noncardioembolic thrombi (10, 11). Thus, the pathological findings of cardioembolic and noncardioembolic thrombi remain controversial. In addition, the proportion of fibrin/platelets and erythrocytes cannot be quantified in all hospitals, including our own, due to the need for special equipment. More convenient methods for distinguishing between cardioembolic and noncardioembolic thrombi are required.

The pathological identification of foamy cells in endovascularly removed thrombi may help to accurately diagnose atheroembolisms, including aortogenic embolic stroke. Thrombus formation from an atheroembolism is closely related to atherosclerosis (12, 13). At an early stage of atherosclerosis, low-density lipoprotein particles enter the arterial wall. These accumulated low-density lipoprotein particles are phagocytosed by macrophages, forming foamy cells. When vulnerable plaques rupture, the thin fibrous caps are torn, and the lipid-rich necrotic core, containing foamy cells or cholesterol clefts, ruptures into the lumen. Because this rupture causes the formation of thrombi, the thrombi may contain foamy cells. In contrast, the formation of cardioembolic thrombi is not associated with atherosclerosis (14, 15), so foamy cells in an endovascularly removed thrombus strongly suggest an atheroembolism. Our case indicates that pathological identification of foamy cells in an endovascularly removed thrombus may lead to an accurate diagnosis of atheroembolism.

The accurate diagnosis of aortogenic embolic stroke using pathological findings from removed thrombi is clinically important with respect to predicting the risk of recurrent embolic stroke. Previous studies have shown that CAAs are associated with an increased frequency of recurrent embolic stroke (3, 16), even in patients with AF (2). Patients with both CAAs and AF should therefore be followed up carefully because of the high risk for recurrent embolic stroke. In addition, an accurate diagnosis using pathological findings from removed thrombi may be clinically important for selecting appropriate medication. A retrospective study of patients with CAAs found that statin treatment was independently protective against recurrent stroke (17). Anticoagulant therapy is useful in practice for the prevention of embolic stroke due to both AF and CAAs. In this case, apixaban was expected to prevent recurrent aortogenic embolic stroke; however, the optimal antithrombotic strategy

for aortogenic embolic stroke with AF has yet to be determined (18). Further studies will be needed in order to identify the optimal antithrombotic therapy for these cases.

In conclusion, we herein report a case of aortogenic embolic stroke diagnosed using pathological findings from an endovascularly removed thrombus and confirmed by an autopsy. The pathological examination of removed thrombi appears to be valuable for the identification of stroke etiology. Removed thrombi should be pathologically examined even if cardioembolic stroke is clinically suspected.

The authors state that they have no Conflict of Interest (COI).

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